# Chapter 18

Pain

* Nociceptive pain
  + Injury to tissues
  + Described as
    - Somatic pain (sharp, localized sensation)
    - Visceral pain (Generalized dull, throbbing, or aching sensations)
* Neuropathic pain
  + Injury to the nerves
  + Burning, shooting, or numbing pain
  + Difficult to manage
* Mechanism of pain
  + Stimulation of pain receptors, nociceptors(free nerve endings)
  + Nerve impulse is sent to the spinal cord by two sensory neurons
    - Aδ fibers
      * Thinly wrapped in myelin
      * Signals sharp, well-defined pain
    - C fibers
      * Unmyelinated
      * Carry information slowly
      * Signals dull, poorly localized pain
  + Neurotransmitters are responsible for transmitting the message along
  + Substance P
    - A neurotransmitter responsible for continuing the pain message
    - May be affected by other neurotransmitters released from neurons
  + Spinal neurotransmitters
    - Critical
    - Control whether pain signals continue to the brain
  + Endogenous opioids
    - Involves endorphins, dynorphins, and enkephalins

Opioids

* Natural or synthetic morphine-like substance
* Acts centrally
* Reduces moderate to severe pain
* Is an narcotic substance (they produce numbness or stupor-like symptoms)
* High first-pass effect
* Interact with at least 6 receptors
  + Mu (type 1 and 2)
    - Activates
      * Analgesia
      * Decreased GI motility
      * Euphoria
      * Physical dependence
      * Respiratory depression
      * Sedation
  + Kappa
    - Activates
      * Analgesia
      * Decreased GI motility
      * Miosis
  + Sigma
  + Delta
  + Epsilon
* Mu and Kappa are the most important for pain management
* Mixed opioid agonist-antagonist
  + Activates one receptor and blocks another
* Use
  + Controls pain
  + Suppress the cough reflex
  + Slows the motility of the GI tract (for cases of severe diarrhea)
  + Sedation
* Side Effects
  + Respiratory depression
  + Sedation
  + Nausea/vomiting

Morphine

* Binds with mu and kappa
* Causes
  + Euphoria
  + Constriction of the pupils
  + Stimulation of cardiac muscle
* Use
  + Relief of serious acute/chronic pain
  + Preanesthetic medication
  + Relieve shortness of breath associated with
    - MI
    - HF
    - Pulmonary edema
* Adverse Effects
  + Dysphoria (restlessness, depression, anxiety)
  + Hallucinations
  + Nausea
  + Constipation
  + Dizziness
  + Itiching
  + Overdose
    - Severe respiratory depression
    - Cardiac arrest
  + Cross tolerance to other opioids
* Contraindications
  + Gallbladder disease
    - Intensify or mask the pain
    - Acute/severe asthma
    - GI obstruction
    - Severe hepatic or renal impairment
* Overdose treatment
  + IV naloxone (most preferred)
  + Activated charcoal
  + Laxatives

Opioid Antagonists

* Prevent the effects of opioid agonists
* Competes with opioids for access to the receptor
* Reverses the symptoms of opioid addiction, toxicity, and overdose
* Can diagnose overdose
* Naloxone (Narcan)
  + Reverses respiratory depression and other overdose symptoms

Opioid Dependence Treatment

* Withdrawal
  + Extremely uncomfortable symptoms
  + Convince user to continue drug taking to avoid the suffering
  + Abrupt discontinue of drug: About 7 days of withdrawal symptoms
  + Intense cravings of psychologic dependence occur for many months/years
  + Treatment
    - Switch patients to oral methadone(Dolophine) [Methadone maintenance]
      * Does not cause the euphoria
      * Does not cure the dependence
      * Avoids withdrawal symptoms
      * Allows patient to return to productive work and social relationships without the physical, emotional, and criminal risks of illegal drug use
    - Administer buprenorphine (Subutex)
      * Sublingual
      * Mixed opioid agonist-antagonist
      * Used early in opioid abuse therapy to prevent withdrawal

Naloxone (Narcan)

* Blocks mu and kappa receptors
* Reverses overdose symptoms within minutes
* Immediately cause opioid withdrawal symptoms in dependent patients
* Use
  + Complete or partial reversal of opioid effects in emergency situations
* Adverse effects
  + Loss of pain relief
  + Inceased blood pressure
  + Tremors
  + Hyperventilation
  + N/V
  + Drowsiness
* Overdose treatment
  + Oxygen
  + IV fluids
  + Vasopressors

NSAIDs

* Inhibiting pain mediators at the nociceptor level
* Bradykinin: associated with the sensory impulse of pain
* Prostaglandins
  + Induce pain through the formation of free radicals
  + Causes inflammation
* Inhibits cyclooxygenase (responsible for the formation of prostaglandins) and inflammation and pain are reduced
* For mild to moderate pain and pain associated with inflammation
* Also have an antipyretic and anti-inflammatory effect
* Aspirin, Ibuprofen, COX-2 Inhibitors
  + Safe
  + Inhibit COX-1 and COX-2 which help form prostaglandins
  + COX-2 more specific for the synthesis of inflammation
* Acetaminophen
  + Prototype antipyretic
  + Reduces fever with an direct action of the hypothalamus
  + Causes dilation of peripheral blood vessels
  + Enables sweating and dissipation of heat
  + Alternative to of aspirin or ibuprofen
  + Doesn’t produce GI bleeding or ulcers or cardiotoxicity
  + Risk of hepatic toxicity with large doses

Migraines

* Throbbing or pulsating pain
* Preceded by an aura (sensory cues)
* Accompanied by nausea/vomiting
* MSG is a trigger found in
  + Asian food
  + Red wine
  + Perfumes
  + Food additive
  + Caffeine
  + Chocolate
  + Aspartame
* Drug therapy
  + Stop or prevent migraines
  + Anitmigraine durgs
    - Triptans
    - Ergot alkaloids
    - Both are serotonin (5HT) agonists
  + Termination
    - Acetaminophen or NSAIDs
    - Triptans (if OTC meds doesn’t work) [sumatriptan (imitrex)]
      * Constricting certain intracranial vessels
    - Ergot Alkaloids
      * For patients unresponsive to triptans
      * Produce multiple actions and side effects
      * Pregnancy category X
  + Prophylaxis
    - Initiated only if the incidence of migraines is high and patient is unresponsive to the other drugs used to abort them
    - Beta blocker propranolol (inderal)
      * Most common
    - Amitriptyline (Elvail)
      * Anti-depressant
      * Preferred for patient who also have a mood disorder or suffer from insomnia

Sumatriptan (Imitrex)

* Causes vasoconstriction of cranial arteries
* Selective (doesn’t affect overall BP)
* Adverse effects
  + Cardiac ischemia
  + Hypertension
  + Dysrhythmias
  + MI
  + Dizzines
  + Drowsiness
  + Warming sensation
* Contraindications
  + Patients with MI, history of angina, hypertension, or diabetes
* Overdose treatment
  + Drug therapy for symptoms
    - Weakness
    - Lack of coordination
    - Watery eyes and mouth
    - Tremors
    - Seizures
    - Breathing problems